

NTP BOARD OF SCIENTIFIC COUNSELORS HIGH THROUGHPUT SCREENING WORKING GROUP

Purpose

The NTP envisions that over the next decade our rapidly expanding knowledge of the physiological, biochemical, and molecular bases of disease will lead to the development of, and a gradual transition to, higher throughput methods for predicting the toxicological impacts of environmental agents. Thus, the NTP plans to build a testing program using less expensive, higher throughput, alternative assays for screening a large number of substances and establishing priorities for additional, more extensive agent-specific mechanistic studies.

The concept of high throughput screening (HTS) is based on the use of automated processes to evaluate hundreds to thousands of agents rapidly for activity within *in vitro* biological systems under a variety of conditions. HTS may also be used to test complex mixtures or combinations of experimental conditions not testable in classical *in vivo* assays. The assays will target the key pathways, molecular events, or processes linked to carcinogenicity and/or reproduction/development endpoints. The NTP anticipates that these assays will use a wide range of exposure concentrations and both human and animal materials (cells, tissues, genes, receptors, etc.) to aid in extrapolating from animals to humans and from high to low exposures. Mechanistic endpoints initially targeted by the HTS program may include genotoxicity, cytotoxicity, cell proliferation, apoptosis, and critical receptor-mediated activities for which, ideally, commercially available assays may already exist; new assays may be developed and automated at NTP contract laboratories.

In order to gain scientific input on HTS and its application for the NTP testing and research program, the NTP will establish the High Throughput Screening Working Group of the NTP Board of Scientific Counselors (“the HTSWG”). The HTSWG will be a technical advisory body to provide a structured and formal mechanism for bringing knowledgeable experts together to address the development and use of HTS by the NTP in its testing and research program. Specifically the HTSWG will provide advice to the NTP Board of Scientific Counselors on HTS.

Function

The HTSWG shall provide guidance and advice to the NTP Board of Scientific Counselors on the development and selection of assays and procedures to be used for HTS, as well as the development of interpretative models for using HTS data to predict human or animal responses with acceptable accuracy. Once the program has been implemented, the HTSWG shall conduct periodic reviews advising on the overall merit and quality of the activities and whether the data generated can be used for predicting the toxicological impacts of environmental agents. Members may also assist in the identification of an initial set of chemicals to test by HTS.

Structure

The HTSWG shall consist of a Chairperson (a current member of the NTP Board of Scientific Counselors) appointed by the Director of the NTP and up to 10 scientists drawn from industry, academia, or government with expertise in, but not limited to, mechanisms of carcinogenicity, reproduction/development, development of *in vitro* assays, high throughput testing systems, chemistry, informatics and data management, computational toxicology, gene expression, cell cycle control and apoptosis, oxidative stress, and receptor biology.

The NTP Liaison and Scientific Review Office within the Office of the Director of the Environmental Toxicology Program will provide management and support services to the HTSWG.

Meetings

The working group is expected to meet annually or at the call of the Chair as need dictates. A government official shall be present at all meetings. The NTP will make the HTSWG meetings as accessible as possible to the public and follow appropriate National Institutes of Health (NIH) guidelines for the management, oversight, and conduct of working groups. The Chair will report on the activities of the HTSWG to the NTP Board of Scientific Counselors on a regular basis.

Compensation

HTSWG members shall be paid at a daily rate equivalent to that of members of the NTP Board of Scientific Counselors, plus per diem and travel expenses. Members who are officers or employees of the U.S. government shall not receive compensation for service.

Termination

The HTSWG shall continue its activities until deemed by the NTP Board of Scientific Counselors as no longer necessary with approval by the Government official.